A Multistate Outbreak of Hepatitis A Caused by the Consumption of Raw Oysters

ABSTRACT

Background. In August 1988 we investigated a multistate outbreak of hepatitis A caused by Panama City, Florida, raw oysters.

Methods. Cases of hepatitis A (HA) with onset in July–August 1988 were identified among persons who ate seafoods harvested in the coastal waters of Panama City, Florida. We conducted a case-control study, using eating companions of case-patients, and calculated attack rate (AR) per 1000 dozen raw oysters served. Enzyme immunoassay (EIA) and a polymerase chain reaction (PCR) technique were performed on samples of raw shellfish obtained from Panama City coastal waters.

Results. Sixty-one case-patients were identified in five states: Alabama (23), Georgia (18), Florida (18), Tennessee (1), and Hawaii (1). We found an increased risk of HA for raw oyster eaters (odds ratio = 24.0; 95% confidence interval = 5.4–215.0; $P < .001$). The AR of HA in seafood establishments was 1.9/1000 dozen raw oysters served. The EIA and PCR revealed HA virus antigen and nucleic acid in oysters from both unapproved and approved oyster beds, in confiscated illegally harvested oysters, and in scallops from an approved area.

Conclusions. The monitoring of coastal waters and the enforcement of shellfish harvesting regulations were not adequate to protect raw oyster consumers. More emphasis should be placed on increasing public awareness of health hazards associated with eating raw shellfish. (*Am J Public Health.* 1991;81:1268–1272)

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Introduction

The consumption of raw or undercooked shellfish has caused numerous outbreaks of bacterial and viral enteric diseases worldwide.[1–18] In the United States, outbreaks of hepatitis A (HA)[4–8] and of Norwalk gastroenteritis[15–17] caused by the consumption of raw shellfish have been reported regularly since 1962, and raw or undercooked clams or oysters were implicated as the most frequent vehicle of infection.[4–8,13–17] To prevent the occurrence of such outbreaks, many states have adopted regulations to prevent the harvesting and distribution of shellfish contaminated by human fecal pathogens.[19] However, these regulations have not prevented raw shellfish–borne outbreaks of HA[8] and Norwalk virus gastroenteritis.[16,17] These outbreaks were linked to shellfish by epidemiologic data; however, to our knowledge hepatitis A virus (HAV) has not been identified in implicated shellfish during outbreaks in the United States.

We describe a large multistate outbreak of HA caused by the consumption of Florida raw oysters. During this outbreak we were able to identify HAV in illegally harvested oysters that we believe were the source of infection, using an enzyme immunoassay (EIA) and in vitro nucleic acid amplification, a method potentially applicable to monitoring the microbiological suitability of shellfish intended for human consumption.

Methods

Background

In early August 1988, cases of HA were reported among Alabama patrons of Panama City, Florida, seafood restaurants and oyster bars. Panama City, located on the Gulf of Mexico, is surrounded by three bays (East, West, and North Bay) where shellfish, particularly oysters, grow naturally. Registered fishermen harvest oysters according to a management plan monitored by the Florida Department of Natural Resources. Oyster beds are classified as approved, conditionally approved, or prohibited for harvesting according to factors such as rainfall, water salinity, and water coliform counts. For 7 years before 1988, the bays surrounding Panama City were closed to oyster harvesting each year from June 1 to August 31. However, in 1988, summer harvesting was permitted in North Bay.

Epidemiologic Investigation

A case of HA was defined as a person who was IgM antibody positive to HAV, or who was diagnosed with HA by a physician during July or August 1988, and

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who had attended a seafood event 10–50 days before symptom onset. Cases were ascertained by contacting neighboring states, all local Florida health departments, and Panama City hospitals and physicians, and through interviews with case-patients and managers of seafood establishments.

We conducted a case-control study in August 1988. All case-patients reached by telephone were included in the case group. The non-ill meal companions named by each patient (0 to 3 companions named per patient) were included in the control group if they did not develop any symptom of HA during the 10- to 50-day period following the seafood meal, if they did not report a past history of HA or jaundice, and if they had not received immune globulin during the previous 3 months. Serum specimens were not obtained to detect asymptomatic infection among controls. A standardized questionnaire was used for telephone interviews with cases and controls to ascertain health status and food consumption during the seafood event.

The direct and indirect costs of the outbreak were estimated from medical information obtained during the case-control study. Direct cost was calculated using mean routine medical fees at local hospitals; indirect cost was calculated at a mean salary of $100 per day of work lost.

To estimate attack rates (ARs) for oyster bar patrons, we reviewed oyster invoices and records in Panama City seafood establishments where patients had eaten. ARs were calculated per 1000 dozen raw oysters served by week and by establishment.

Crude odds ratios (OR) and 95% exact confidence intervals (CI)[20] were calculated for each food and exposure investigated. Statistical tests used included χ^2 with Yates correction, the two-tailed Fisher exact test, the χ^2 for trend, and the Student t test for continuous variables. When case-patients had eaten in more than one restaurant during the exposure period, the analysis of data was restricted to the restaurant which had reported other case(s) being exposed on the same day.

Environmental Investigation

We traced the origin of oysters by reviewing oyster bag tag numbers recorded by seafood establishments. Information on illegal oyster harvesting activities in Panama City coastal waters was obtained from the Florida Marine Patrol. Coliform count records from shellfish growing areas and at a sewage treatment plant (plant A) were reviewed. We inspected Panama City approved and unapproved oyster growing areas to search for sources of fecal pollution and collected samples of oysters and water from approved (North Bay) and two unapproved areas (Watson and Beatty Bayou), scallops from a scallop growing area (Shell Island), and sludge from another sewage treatment plant (plant B) located in Watson Bayou. We also obtained frozen raw oysters that had been illegally harvested in Watson Bayou in early August 1988 and confiscated by the Florida Marine Patrol.

Laboratory Investigation

Coliform counts were done on water and oyster meat samples using the three tube five dilution technique.[21] For the detection of HAV antigen and nucleic acid, individual shellfish (oysters and scallops) were removed from the shell; the digestive tract, mantle, and muscle were minced; and material from two specimens was pooled, homogenized in phosphate buffer saline + 0.1M ethylene diamine tetra acetate (EDTA), and clarified by centrifugation. Separate instruments were used to prevent cross-contamination of specimens. Supernatants of the homogenated shellfish were tested for HAV antigen using a previously described EIA.[22] HAV was quantitated from a standard curve prepared from cell culture–derived HAV, strain HAS-15,[23] and diluted in oyster meat homogenate supernatant fluid from oysters not implicated in an illness outbreak. Sludge samples from the sewage treatment plant were prepared as a 10% (w/v) suspension, sonicated, and clarified by centrifugation, and the supernatant was tested for HAV antigen.

Specimens (resuspended homogenate pellets, homogenate supernatant, and sludge) were tested for HAV-RNA by in vitro nucleic acid amplification using the polymerase chain reaction (PCR). HAV-RNA was obtained by immunocapture of virus with the capture antibody used in the HAV-Ag EIA[24] followed by heating at 900°C in reverse transcriptase buffer for 3–5 minutes. The oligonucleotide primer complementary to HAV-RNA was annealed at 90°C for 3 minutes, cooled on ice, and cDNA was synthesized at 42°C for 1 hour with 200 μmoles dNTP's, 5 units AMV reverse transcriptase, and RNAscin.[25] The second primer was added and HAV-cDNA was converted to double-stranded DNA and amplified with a heat stable (Taq) polymerase in a thermal cycler for 30 cycles (DNA Thermal cycler, Perkin-Elmer Cetus, Norwalk, Conn). Amplified nucleic acid products were analyzed by electrophoresis at 10 volts/cm on a horizontal gel (Hoefer Scientific Instruments, San Francisco, Calif) in a composite agarose gel of 3% NuSieve and 1% Sekem (FMC Bioproducts, Rockland, Md) prepared in Tris-borate-EDTA buffer containing 0.5 μg/ml ethidium bromide. DNA specific for the amplified region of the HAV genome was identified by hybridization using a 32P kinase-labeled oligonucleotide probe that was internal to the two limiting primers used in the PCR.[25]

Results

Epidemiologic Investigation

Sixty-one case-patients were identified; all but two had been tested and were IgM anti-HAV positive. Of 53 patients interviewed, all but 1 stopped working while ill and 17 (32%) were hospitalized (range = 2–21 days, median = 4 days). The duration of illness ranged from 7 to 49 days (median = 21 days), and the median number of visits to a physician while ill was four per patient (range = 1–13 visits). There were no deaths; seven secondary cases occurred among household contacts of case-patients. The total cost of the outbreak was approximately $200 000: $73 000 for direct costs, i.e., medical care and the outbreak investigation, and $130 000 for indirect costs associated with lost work days.

Illness onset ranged from July 4 to August 15 (Figure 1), the exposure period from June 3 to July 21, and the incubation period from 16 to 48 days (median = 29 days). Case-patients lived in Alabama (23 persons), Georgia (18), Florida (18), Tennessee (1) and Hawaii (1). Case-patients ate in seafood restaurants or oyster bars in Panama City (53 persons, 86.9%), in a restaurant in Alabama that served oysters harvested in Panama City (3; 4.9%), and at private family gatherings in Panama City (5; 8.2%). Age of patients ranged from 8 to 60 years (median age = 31 years), and 49 (80.3%) were male.

Fifty-three case-patients and 64 controls were enrolled in the case-control study. Cases tended to be younger than controls (mean age = 27.5 and 32.2 years, respectively; $P = .02$) and were more likely to be male (81 vs 39%; $P < .001$). The risk of HA was greater for patrons who ate raw oysters than for patrons who did not (OR = 24.0; $P < .001$) (Table 1) and increased with the number of raw oysters ingested (Table 2). Of the two case-patients who did not eat raw oysters, one ate baked oysters, and the other ate raw

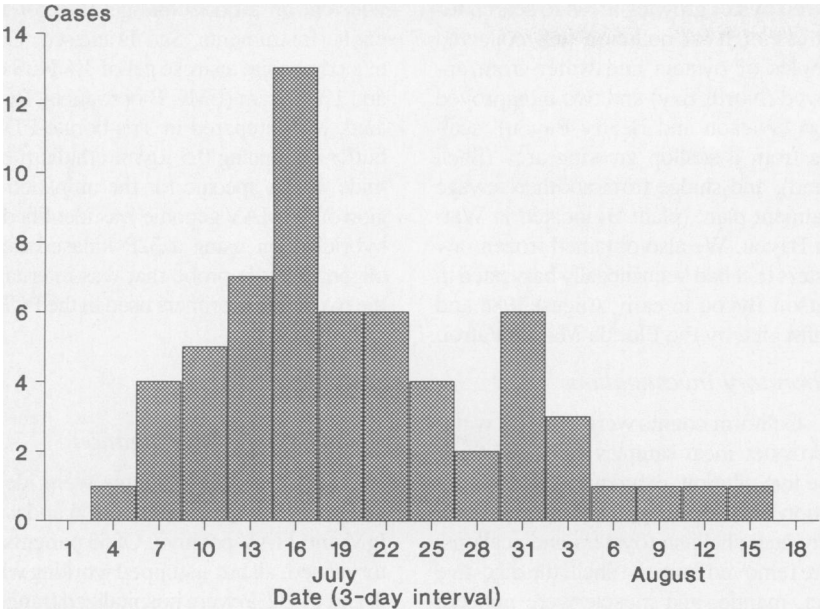

FIGURE 1—Cases of hepatitis A by date of onset, oyster associated hepatitis A outbreak, Florida, July–August 1988.

TABLE 1—Seafoods Consumed by Case-Patients and Controls, Oyster-Associated Hepatitis A Outbreak, Florida, July–August 1988

Seafood	Cases (n = 53) No.	Cases (n = 53) %	Controls (n = 64) No.	Controls (n = 64) %	Odds Ratio	95% CI[a]	P
Raw oysters	51	96	33	52	24.0	5.4–214.7	<.001
Fried or baked oysters	7	13	13	20	0.6	0.2–1.8	.4
Steamed oysters	1	2	5	8	0.2	0.01–2.1	.2
Raw shrimp	3	6	1	2	3.8	0.3–201.5	.3
Cooked shrimp	17	32	30	47	0.5	0.2–1.2	.1
Steamed clams	1	2	3	5	0.4	0.01–5.1	.6
Fish	17	32	18	28	1.2	0.5–2.9	.8

[a]CI = confidence interval.

TABLE 2—Number of Raw Oysters Eaten by Oyster-eating Case-patients and Controls, Oyster-Associated Hepatitis A Outbreak, Florida, July–August 1988

Number of Raw Oysters Eaten	Cases (n = 51) No.	Cases (n = 51) %	Controls (n = 33) No.	Controls (n = 33) %	Odds Ratio	95% CI[a]
1–6	6	12	18	55	1.0	—
7–12	20	39	11	33	5.5	1.5–21.5
>12	25	49	4	12	18.8	3.9–99.3

χ^2 for trend=20.0, $P < .001$.
[a]CI = confidence interval.

scallops caught at Shell Island beach. No other food items were associated with illness (Table 1), and the number of raw oysters eaten (>12 vs <12) had no effect on incubation period (<30 days; 55% vs 48%; rate ratio [RR] = 1.1; $P = .9$), duration of illness (>20 days; 79% vs 74%; RR = 1.1; $P = .9$), or hospitalization rate (29% vs 33%; RR = 1.1; $P = .9$).

During the exposure period, the 11 Panama City establishments associated with cases served approximately 27 900 dozen raw oysters. The median amount served per week was 3500 dozen (range = 1950–4800) (Figure 2), and the median number served by each establishment was 1994 dozen (range = 1050–8230). The overall AR was 1.9 cases per 1000 dozen raw oysters served with a peak during the third week of June (Figure 2). ARs by establishment ranged from 0.1 to 18 cases per 1000 dozen raw oysters, and most case-patients (44/52; 84.6%) had eaten raw oysters in one of four restaurants (A–D, Table 3).

Environmental Investigation

Seafood establishments and private individuals purchased raw oysters from wholesalers who obtained most of their oysters from Panama City–registered fishermen. Panama City bays met the defined safety standards at the time they were opened. Information gained from the Florida Marine Patrol indicated that illegal oyster harvesting at night was common during the summer of 1988, particularly in Watson Bayou where bootleggers arrested in early August had obtained multiple bags that they sold directly to some restaurants and oyster bars in Panama City.

Inspection of Watson Bayou showed failing septic tanks, boat sewage disposal, and sewage treatment plant sludge in proximity to unapproved oyster beds. Review of coliform counts at the effluent outfall of sewage treatment plant A was high [>16 000 most probable number (MPN)] from March through April 1988 and again in July, but not during May and June. This plant discharged approximately 1 mile from Watson Bayou.

Laboratory Results

Coliform counts higher than the maximum allowed were found in the water of two unapproved beds, although the oyster meat of only one of the beds was abnormal, and no human fecal pollution was detectable in the approved areas (Table 4). One of the three oyster pairs from approved beds of North Bay, all four scallops obtained from Shell Island, two oyster pairs from one of the beds sampled in Watson Bayou, and Watson Bayou oysters confiscated from a bootlegger were positive for HAV antigen by the EIA. HAV-RNA was detected by PCR in all oyster samples positive for HAV antigen

by EIA (Table 4). However, two oyster samples HAV antigen negative by EIA were positive for HAV-RNA by PCR including a sample from Beatty Bayou, which was unapproved, and a sample from North Bay approved oyster beds (Table 4). Suspensions of sludge obtained from the sewage treatment plant were negative for HAV antigen and for HAV-RNA by PCR.

Discussion

This oyster-borne outbreak of HA is the largest reported in the United States since the 1973 Louisiana outbreak that involved 263 cases.[8] Although all case-patients recovered from their illness, the economic burden of the outbreak was high.

The risk of illness increased with the number of raw oysters consumed, suggesting a dose-response effect. However, there was no relationship between the quantity of raw oysters consumed and the incubation period, the duration, or the severity of illness. These findings suggest that the number of oysters eaten increased the chance of eating an infectious oyster rather than increasing the amount of virus ingested, which has been shown to decrease the incubation period.[26]

Although the case-control study showed that males had a greater risk of HA, this association is probably related to the use of eating companions of case-patients as controls: Florida adult males are more likely to eat raw oysters than females (Florida Behavioral Risk Factor Survey, Department of Health and Rehabilitative Services, unpublished data, 1988) and therefore to develop oyster-borne HA. Thus, controls as meal companions of case-patients were more likely to be females (spouse or girl friend).

Although the environmental investigation was not successful in definitively identifying the origin and the distribution of the contaminated oysters, we believe that contaminated oysters illegally harvested from unapproved waters were responsible for the vast majority of cases. However, we cannot exclude the possibility that some cases may have been caused by contaminated oysters harvested from approved beds of North Bay because both EIA and PCR identified HAV in oysters sampled there. Nevertheless, several factors strongly suggest that this outbreak was the result of bootlegging. First, because North Bay is the most common source of raw oysters served in Panama City, the observation of higher ARs of HA in four establishments suggests that more contaminated oysters were sold in those four establishments than in the other establishments. Second, according to anecdotal reports, many oysters had been illegally harvested from Watson Bayou in June and July 1988 and sold to specific seafood establishments in Panama City. Third, HAV was identified in oysters obtained directly from Watson Bayou and in oysters confiscated from a person who was arrested for illegal harvesting there. We also believe that the opening of Panama City coastal waters to summer harvesting after 7 years of summer closure facilitated the sale of the locally bootlegged oysters.

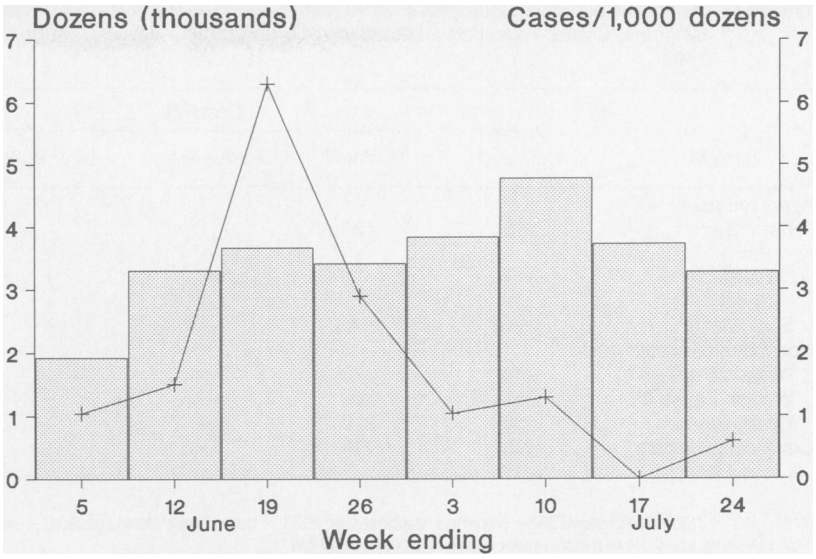

FIGURE 2—Raw oysters served (bar) and attack rate of hepatitis A per 1000 dozen raw oysters served (line) by week of exposure, oyster-associated hepatitis A outbreak, Florida, June–July 1988.

TABLE 3—Hepatitis A Attack Rate by Panama City Seafood Restaurants or Oyster-Bars[a] of Raw Oyster Consumption, Oyster-Associated Hepatitis A Outbreak, Florida, July–August 1988

Restaurant	No. of Cases	Cases per 1000 Dozen Raw Oysters
A	24	18.0
B	9	5.4
C	6	2.5
D	5	1.1
Others[b]	8	0.4
All	52	1.9

[a] n = 11.
[b] n = 7.

The raw scallops, eaten by one case-patient not exposed to oysters, were harvested off Shell Island where scallops were also found to contain HAV. This area is approximately 5 miles downstream from Watson Bayou, and a common source of fecal pollution may explain the contamination of shellfish from both locations.[14,15,18,27]

In the past, the isolation of viral pathogens from shellfish implicated in disease outbreaks has been difficult.[27] The finding of HAV by immunoassay in oysters obtained from the various harvesting areas indicated high levels of contamination. Even in the approved areas, oyster and scallop samples were positive for HAV by either or both EIA and PCR, which suggests that contamination may have been more widespread than was originally suspected. Virus isolation by cell culture was not attempted because of the extreme difficulty in growing wild-type HAV from environmental samples.[28] While direct proof of infectivity of either HAV-antigen or HAV-RNA positive oysters was not obtained, the epidemiologic evidence for infectivity was substantial, and it has been shown that HAV remains viable for long periods of time in water.[28]

The application of rapid viral diagnostic methods (EIA or PCR) for the identification of HAV and presumably other viral pathogens in shellfish has the potential for assuring the quality of this raw food product. However, these methods must be verified by infectivity studies in cell cul-

TABLE 4—Coliform Counts and Hepatitis A Virus Identification in Water and Shellfish Samples, Oyster-Associated Hepatitis A Outbreak, Florida, July–August 1988

Sample	Water Coliform[a]	Shellfish Coliform[b]	Shellfish HAV-EIA	Shellfish HAV-PCR
Approved areas				
North Bay[c]	13	<20		
Pair 1			+	+
Pair 2			−	+
Pair 3			−	+
Shell Island[d]	NA	NA	+	+
Nonapproved areas				
Watson Bayou 1[c]	240	170	+	+
Watson Bayou 2[c]	NA	NA	−	−
Beatty Bayou[c]	30	330	−	+
Confiscated oysters	NA	NA	+	+

Note: HAV = hepatitis A virus; EIA = enzyme immunoassay; PCR = polymerase chain reaction; + = positive test result; − = negative test result; NA = not available.
[a]Most probable number per 100 cc; maximum level permitted for water is 14 per 100 cc.
[b]Most probable number per 100 g; maximum level for shellfish is 230/100 g.
[c]Oysters.
[d]Scallops.

ture or nonhuman primates. This outbreak points out the failures of current regulations in assuring the quality of raw shellfish because enforcement cannot effectively prevent illegal harvesting, and it suggests that even approved areas may be contaminated with HAV. Emphasis must be placed on increasing the public awareness of the health risks associated with the consumption of raw or undercooked shellfish. □

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